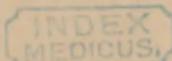


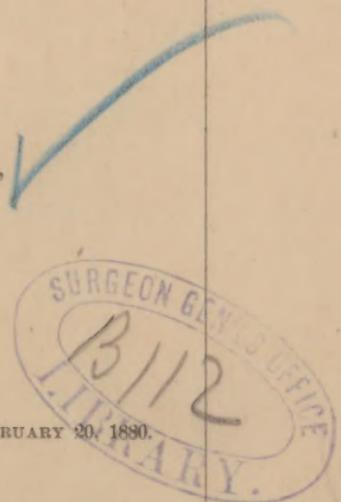
CLEVENGER (S. V.)

THERAPEUTIC
ACTION OF MERCURY.

INAUGURAL THESIS READ BEFORE THE CHICAGO
BIOLOGICAL SOCIETY, FEBRUARY 4, 1880.



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ACTION OF MERCURY.

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BY S. V. CLEVENGER, M.D., CHICAGO.

The present condition of the therapeutics of mercury is summed up by Bache in the last U. S. Dispensatory, page 482, in these words: "Of the modus operandi of mercury we know nothing, except that it probably acts through the medium of the circulation, and that it possesses a peculiar alterative power over the vital functions, which enables it in many cases to subvert diseased actions."

The general idea pervading the literature of the subject is that some unknown compound is formed by the metal and its salts in the system. Mailhe claimed that the bichloride was formed in the stomach, but failed to establish his theory. Maisch, Buchheim, Oettingen, Winkler and Jeannel dissent from Mailhe's view, and Jeannel suggests the probable formation of the black oxide in the alimentary canal. Maisch denies that this takes place, or that the black oxide occurs in old pill masses. M. Sée published arguments in favor of an albuminate of mercury as the active agent elaborated in the body. Odling thinks the mercury acts as a red blood globule in carrying oxygen to tissues. Had any one of these views been established it would have explained nothing. The mystery would have been no nearer solution. Investigators seem to have been lured away from the evident and fundamental in imagining no connection between the simple, easily-discriminable physical properties of mercury and its therapeutical effects, assigning the drug occult, catalytic properties.



Physiologists do not disregard the mechanical properties of water, yet mercury, to a certain extent its congener, seems never to have been considered from this standpoint. Both water and mercury are fluid at common temperatures, both vaporize at all temperatures; both change their specific gravities in passing from solid to fluid and thence to vaporous conditions; both maintain extreme division of their particles, under certain circumstances, and by loss of heat or under compression cohere in drops and fall. The great difference is that mercury is fourteen times heavier than water and has a different solidifying point.

No one disputes the fact that blue mass contains minutely divided mercury, but nowhere have I been able to find any speculations upon the probability that the *mercury* itself thus given was able to accomplish its well-known effects. Histological tissues and a finely divided metal have not been considered as amenable to ordinary mechanical principles. The fact of both being microscopic at once relegated them to mysterious modes of working, though every one acknowledges that a billionth of an inch is no less an entity than is a billion miles. When the metal, in an undivided or uncombined state, is administered, it rapidly passes through the intestines, with apparently no effect whatever. The cohesive properties of its component particles resist separation. Considerable trituration with an excipient is necessary to reduce the metal to globules; shaken up in water an uneven but pretty fine division may be made, but eventually the fluid metal runs together again, the water opposing only temporary resistance to the metallic confluence. Honey, fats, oils, confections, etc., when mixed with the fine globules, tend to keep the particles apart. I found that albumen and glycerine would effect a separation better than many substances. Finely divided, mercury presents a grayish appearance, passing into black as the division is made

extreme, this condition favoring the reverberations of light from particle to particle until no rays are reflected to the eye. The microscope reveals that no change from the metallic state has occurred in reducing the metal to this form. To count the globules in a gram (15.4 gr.) of blue mass I spread it mixed with water over a square decimeter of surface and found an average of 2,000 visible under a very low magnifying power in an area of a square centimeter, which would make 200,000 of these globules in a gram. But under an objective magnifying seventy diameters, more than ten times as many became apparent. Dr. Lester Curtis estimated the size of these globules at from $\frac{1}{1000}$ of an inch to sizes almost immeasurably smaller. In a gram of pill mass there is one-third of a gram of mercury, which would cubically measure $\frac{1}{40}$ of a cubic centimeter. Taking .01 millimeter (Kolliker) as the average diameter of the capillaries, the division of this mass into twenty-five million globules would suffice to reduce all the mercury to capillary sizes. But we have seen that all are not so reduced though many are divided up very much smaller. Carpenter, on p. 138 of his *Physiology*, asserts that metallic mercury, finely divided, can be absorbed by the blood vessels from the alimentary canal.

Let us adopt the simple supposition that these minute globules drop unchanged into the glandular tubules and force their way to the blind extremities: necessarily the expulsion of less heavy contents from these tubules would occur regardless as to whether such contents were morbid or normal. In this manner a deobstruent action would be obtained by as simple and effectual means as were we to drop cannon balls into a large pipe. Peristalsis would assist in passing these same globules onward to other secreting and excreting surfaces, and a few globules of the proper size could thus change the conditions of a large area of minute tubules. After passing the pylorus the

simple follicles and duodenal glands could be affected as were the gastric tubules, and by thus cleansing glandular structure restore normal secretion, or, as in some cases, induce hypersecretion. The intestinal villi and lacteals could pass the metal into the circulation, while the portal vein would carry most of it direct to the hepatic parenchyma. Somewhat as the direct aortic connections with the carotid render embolismus most frequent in the left middle cerebral artery, the peculiar relationship of the inferior dental arteries with the external carotids, would facilitate mercury accumulation in the cancellated tissue of the inferior maxillary bone with resulting tenderness and sponginess of gums. The minute globules would find easier ingress to, than egress from, the dependent portion of the lower jaw bone, where they would accumulate to exert a slow but sure disturbing effect upon the gums and incisors, and finally molars. The irritation of the globules upon the peripheral nerves of the salivary glands, together with the deterersive influence of the metal itself, already mentioned, would account for the activity of the sub-lingual sub-maxillary and parotid glands in ptyalism. The question would arise, why should not catharsis continue during ptyalism if all glandular structures were affected; the liver being caused to secrete more bile as the maxillary glands are stimulated to salivary excretion? In the first place the innervation of all glandular structures is not alike, hence they are not comparable in their actions, next ptyalism succeeding catharsis shows that while the liver and intestines evince the first effects of mercurial ingestion, the superior glands are reached later through the circulation. From this it might be reasoned that inunctions of mercury would impress the general system rather than the liver or alimentary canal, and clinically I believe this to have been proven.

“Congestion of the liver, attended with enlarge-

ment of the spleen," according to Maisch and Stille, p. 726, "is followed by excessive salivation and even gangrene of the mouth." The hepatic channels being closed in such cases, remoter glands would inevitably receive the greater portion of the metal.

Mercurials load the circulation and emunctories with effete matter because of their deobstruent effects and ability to insinuate their particles among all tissues, separating the morbid or ulcerated portions from the healthy, by the great and universal law of heavy bodies acting in the line of "least resistance." If the bile is improperly diverted or suppressed, it restores it, by opening the channels through which it normally flows; if superabundant from organic obstruction it would regulate its quantity in the same way by affording exit for morbific causes. Its aplastic action is ascribable to the capillary and lymphatic cleansing its passing would produce; the million minute globules pushing open circulatory channels and preventing accumulation, as well as affording means for absorption. Provisional callus and wound healing would be interfered with by the globules breaking up new tissue and interfering with its formation as would any foreign substance. Mercury has been retorted over in considerable quantities from the bones of those who have died from mercurial cachexia, the little particles finding stopping places in the cancellated tissue removed from more active circulatory influences, and, in excess, doubtless dissecting away the periosteum, filling the lacunæ and canaliculi, thus unavoidably producing caries.

Stille and H. C. Wood quote Eld, Buchner, Cantu, Jourda, Andouard, Fourcroy, Gmelin, Byanon, Mayençon, Bergeret, Saikowsky, Oesterlin and Heller as having found mercury, regardless of the form in which it was taken, in the blood, urine, serum and pus of ulcers, in the saliva, faeces, seminal fluid and aborted foetuses of salivated women. "Indeed in

every conceivable secretion and every tissue." In these quotations the metal alone is spoken of as having been found in these tissues and fluids. Very often the word mercury is used in a loose way by authors to include the salts as well. I can imagine that in these cases the usual chemical tests were applied for the base and the radical was undetermined. The microscope would have been effective enough for the discovery of the metal, but nowhere does any use appear to have been made of this instrument in such investigations. As a sample of the many, Bowman, p. 298, says: "When the presence of mercury is suspected in the viscera or other tissues of the body, the part intended for examination should be first cut into thin slices and heated with hydrochloric acid and chlorate of potash, by which means any mercury that may be present will be converted into the bichloride and thus brought into a state of solution." This method will detect mercury but not the elements with which it has been combined. The microscope should first be resorted to. In another connection Brande and Taylor, p. 491, say: "Globules of the $\frac{1}{8000}$ part of an inch in diameter may be easily recognized by the aid of a microscope. Their perfect sphericity, their silvery whiteness by reflected and complete opacity by transmitted light at once identify them as metallic mercury."

The occasional tonic influence of the metal would follow wherever glandular obstruction was superinducing diminution of the red blood corpuscles, as insomnia may be overcome by bromides removing the cause, while no one assigns the bromides a place among hypnotics.

Mercury is not a tonic; but if it increases secretion, removes obstructions and sets the corpuscular manufacturers in order as it does the biliary, it induces tonicity as the bromides induce sleep.

But mercury also causes anæmia, which might be

expected by persisting in its use, remembering its occlusive powers in closing the minute passages and tubular structures which, in medicinal quantities, removed preëxisting obstructions.

Mercury in larger doses diminishes the number of red blood corpuscles and produces anaemia, emaciation, ulceration, febrile symptoms, with a peculiar "jerking, thready" pulse. Obviously an effect which might be salutary upon the glandular system, wrought by small doses, could become pernicious by over doses, and haematoses be seriously interfered with by the vascular stasis induced by mercurial plugging of the arterioles and venioles. Any irritation causing perversion of the hepatic and splenic functions, certainly could only be followed by haemic degeneration, and I am inclined to think that the pulse characterizing hydrargyria is due to the irregular but frequent propulsion of blood by *vis a tergo* clearing of the lesser vessels where the metallic globules had for a while backed up the current till forcibly overcome. This brings us to the consideration of the nervous phenomena among its toxic effects.

The poison produces ulceration, neuralgic pains, paralysis agitans, epilepsy, often melancholia, all of which can be produced by thrombus, embolus, passive or active cerebral or spinal congestion, directly brought about by what has just been mentioned.

Take any treatise on nervous diseases, and wherever the words clot, thrombus and embolus occur, substitute mercurial accumulation, and the cause is fully explained, as far as I am able to judge. I will go farther, and say that ischaemic softenings of cerebral tissue, infarctus, mania, aphasia; ay, even hemorrhages, have been caused by mercury, often heretofore ascribed to syphilis; not, of course, denying that this disease has not as often produced the same species of disorders.

Thus accumulation in the terminal twigs of the

cerebral cortical arteries would induce paralysis, paresis, softenings, tremors, hemiopia, amblyopia, etc., according to location, and whether the basilar or carotid supply contained the larger quantity of mercury. Should the middle cerebral artery be the meeting place of the molecules, according to subsequent injections of the metal thence, aphasia, hemiplegia or anaesthesia could supervene, singly or together, depending upon whether the gyrus operculum, insula, optic thalamus, corpus striatum, crus or internal capsule had become congested or deprived of blood by this interference.

Bumstead relates a case of epilepsy and general nervous disturbance, in his book, under syphilitic neuroses, which can be better accounted for as mercurialization. The patient (Mr. F.) had been subjected to a long course of mercury, and manifested nervous and mental derangement, quite compatible with the supposition that the mercury was the cause of all the trouble. Bumstead gave him more mercury with iodide of potassium, and was gratified to notice immediate benefit. The iodide alone would have been the better remedy, as iodine unites directly with mercury to form the mercurous iodide. That mercuric iodide is not formed, is evident, from the physiological effects of this active compound not evincing themselves. The less soluble mercurous iodide is carried back into the circulation from the bony or vascular recesses in which the iodine united with the mercury, and decomposing, leaves the mercury to reproduce the same phenomena as when first ingested, with the advantage that the excretory channels have a better chance to eliminate the mercury while circulating than when lying dormant in inaccessible places. This would explain why the iodides re-salivate the mercurialized.

Finding metallic mercury "in every conceivable tissue and fluid of the body" warrants the supposi-

tion that the instances of diabetes, vomiting, gastric and pulmonary irritation following hydrargic exhibition are owing to nerve center irritation mechanical and direct in the floor of the fourth ventricle, or to interference with its blood supply. We might, also, at this stage, expect an augmentation of the salivary flow by irritation of the chorda-tympani nerve, and this may be among the initiatory sialagogic causes. It is a perfectly legitimate view that this irritation may be exerted upon the nerve centers by the heavy globules of the metal, exactly as serous or purulent accumulations may be considered as mechanically productive of nervous and mental derangements, or that mercurial interference with the circulation thereabouts would be followed by such neuroses.

The elimination of mercury from the system seems to be principally through the kidneys: but gold rings, brooches, necklaces, in contact with the person, will become covered with mercury films during a course of hydrargic treatment. Consistently with its vaporizable tendency increasing with heat elevation, warm baths help its passage through the sudoriparous channels, and it is well known that nearer the tropics greater immunity is enjoyed from the effects of large doses. Indeed, the therapeutical dose could be regulated by geographic isothermal lines. The Hot Springs, Arkansas, physicians attribute much of the success in specific ailment treatment there to the climate, which admits of larger doses of the drug. Now, if we take into account the climate and abundance of hot water in that locality, and reasoning that elimination of both mercurials and the specific poison, the evolution of which they assist, is thus greatly facilitated, we have a key to many of the cures effected there, and also to the reappearance of the disorder among those apparently cured who return north, where climatic influences and failure to keep up the hygienic routine, so convenient at the Hot

Springs, had closed the excretory passages upon abated, but still existing, disease.

As to the so-called "specific" reputation of mercury in syphilis treatment, and its modus operandi, I might be excused detailing probabilities until the pathology of the complaint is better understood. The disposition of the virus being to centralize itself upon and destroy certain areas, it seems likely that the metal may, by attacking such weakened points, not only break them down, but prevent the static degeneration necessary for ulcerative processes. This, with the antagonism the metal has for occlusion anywhere except what it induces itself in great doses, would suffice as a tentative view until we demonstrate exactly the cause of both the disease and its cure.

The incendiary can do no harm to society while the police are alert and keep him "moving on." Syphilis, though in the blood, may not manifest itself if sufficient globules are chasing it from forming nuclei; but where the fluids of the body are saturated with syphilitic points enough to produce tertiary symptoms, how futile must any attempt be to restore health by any doses of the drug under consideration. The disease itself is depleting the system at this stage, and mercury but adds to the trouble, having more carious and degenerated spots to work upon.

In short, at this period both syphilis and mercury will fraternize against the body as against a common enemy. Tonics might arrest the cachexia induced by either or both, and in addition the iodides which are known to act both upon this disease and its putative cure should be given.

The author of the toxic effects of mercury in Ziemsen's Cyclopaedia, has made several great mistakes in regard to the chemical and therapeutical properties of the metal, among which are noticeable his statement that hydrochloric acid acts upon mercury, and that calomel always salivates young children. Such

mistakes in a standard work show that instead of its being a compilation of the best literature, each article is but one physician's opinion on a certain subject, and as such should be valued in proportion to its correctness.

"Prof. Fürbringer, of Jena, (Archiv f. Klin. Med.) has made a large number of hypodermic injections of metallic mercury, and states that at the times of the injections they are well borne, but within twenty-four hours inflammatory symptoms set in and frequently result in abscess. If it be simply injected and not divided by subsequent rubbing, no mercury can be found in the urine, but has been obtained as unreduced metal from under the skin at the end of a year and a half. However administered, a slow improvement of the syphilitic symptoms takes place. Metallic mercury is best borne when given in an emulsion; (Hg. 2.00 Mucilage of Acacia and Glycerine at 10.00,) one or two injections per week should be made. Fürbringer believes that this plan of treating syphilis by mercurial emulsion injections should be reserved for cases in which inunctions and internal treatment fail or in which it is not advisable to make frequent injections" (St. Petersburg Med. Wochenschrift). I do not believe this method has a particle of advantage over mercurial inunctions well rubbed in. It is cited merely to show the identity of the results of mercurialization, however administered, and the fact that the mercury was not changed after a year and a half contact with subcutaneous tissue. The reason it was not fully absorbed, was that division had not been effected between the particles of the mass.

Dr. Fessenden N. Otis, in a series of clinical lectures on the physiological pathology of syphilis, published in the Boston Medical and Surgical Journal, January and February, 1880, assumes syphilitic inoculation to consist of contact of a degenerate amoeboid corpuscle, or disease germ, with the healthy

human white blood corpuscle. The lymph spaces and channels convey this poison, multiplied in its course, to the general blood current. He cites Bäumler, in Ziemsen's Cyclopedie, as virtually supporting the view that the characteristic feature of the active syphilitic cell is the possession of ability to set up in other cells through contact the same disposition to rapid proliferation. These cells *obstruct* tissues and undergo degeneration and elimination. Prof. Otis demonstrates the syphilitic tubercle in common with all syphilitic sequelæ to be *a deposit of arrested normal material*. He agrees with both Bäumler and Wagner, in stating that "the favorite seats of these accumulations are in the subcutaneous cellular tissue, the skin, in and upon the bones, the liver, the testicles, brain, kidneys, and, especially in children, in the lungs. They occur as infiltrations of microscopic size scattered through the parenchyma of an organ." The causes of the accumulations, Otis claims, are the "*interferences with the lymphatic circulation*, the natural channels through which, according to Rindfleisch, the nutritive material exuded into the tissues in excess of the necessities of growth and repair is returned to the general circulation. *Luxurious new formations, catarrhs and secretions of all kinds, must be produced when the lymph conveyance is hindered.*" Rindfleisch further says: "we will find this position in pathology very frequently confirmed."

Prof. Otis emphasizes this matter of "*obstruction of lymphatic vessels*," and "*hindrances to the lymph conveyance*," throughout his lectures, by italicizing as above, and I advise earnest consideration of the publications mentioned in connection with this paper.

Notwithstanding its aplastic properties, surgeons employ some of its preparations before an operation, where the subject is syphilitic and there is likelihood of the disease complicating or retarding cicatricial growth. From the mechanical standpoint it would

seem that the surgeon in such cases chose the lesser evil. The aplasticity of syphilis being progressive and destructive, while that of mercury abates, when the cause is withheld, or is even preferable, to the fibrinous degeneration of syphilis.

The percentage of fibrin would be reduced by the increase of the watery secretions attending glandular activity. In this way mercury would be indirectly as well as directly opposed to plasticity.

BLUE MASS.—Under a three-quarter inch objective, magnifying seventy diameters, I placed the web of a frog's foot, and acquainted myself as thoroughly as possible with the peculiarities of its blood vessels, pigment granules, appearances by reflected and transmitted light, and then gave the frog five grains of blue mass. Twenty-four hours afterward I examined the frog, and was surprised to find little globules of mercury mingled with the mucus it had excreted from its skin. Brushing these off, I placed its feet again under the same lens, and found blood vessels choked with metallic mercury; aneurismal and varicose pouches were distended with mercury, and a great number of the so-called pigment granules had changed to a yellow metallic luster; these spots reflected the light as would mercury, when examined by direct rays. As many as twenty of these lacunæ, or star-shaped bodies could be counted between two toes, and altogether there were about a hundred on each foot. The close resemblance between these lacunæ as thus injected, and the description in Stricker of the lymphatic saes in the course of the lymphatics of the frog, led me to believe, at Dr. Lester Curtis' suggestion, that I had observed mercury in the lymphatic channels of the frog. Two little tubules choked with mercury presented a singular phenomenon. Under the power used these tubes appeared blind, but a little globule of unmistakable mercury lay upon the surface of the web at the outer end of one

of the tubes. Watching this globule intently for ten minutes, it suddenly increased in size and the tube collapsed, having emptied its mercurial contents outward. The globule thus formed was twice as large as the characteristic blue mass globule, and was easily removed from the web by a camel's hair pencil. The other similar tube was more curved, and at its outer end had two such globules, both of which increased slowly in size, and in half an hour had grown very large at the expense of the tubular contents, the tube disappearing as did the first mentioned. Nowhere could I see anything like foreign particles *circulating* in the blood. The white and red blood corpuscles were distinctly visible, but in one capillary I found a small, dark particle gradually accumulating similar particles near it; these I suspected were minute mercury globules; they accumulated against the current, and the blood passed around them freely; suddenly the down stream end of the mass broke away and apparently washed away in the blood out of sight. This was repeated several times while the mass, in this way, was proceeding up stream. While exchanging objectives for a higher power, the capillary cleared up. In one vein I observed plainly a large globule of mercury lying motionless, while the blood corpuscles beat against it with as little effect as water would have against a great stone in a brook; the corpuscles changed positions to pass it in the vessel, but slid by as rapidly as ever. Some of the exuded mercury globules on the web enabled me to obtain good comparative measurements. Six of these metallic spheres lay on the surface, just over one of the smallest capillaries. The six together measured the diameter of the capillary, and could easily have passed through this blood vessel abreast.

I repeated the experiment on a smaller frog by anointing the chin, axillæ and thorax with Squibb's

oleate of mercury, with the same result, only the large sized globules were not so numerous. To a third (large sized) frog I gave ten grains of blue mass, and about as much blue ointment. I kept him in a glass jar, to be sure he did not eject the pellets, and in this case, twenty-four hours after, found the lymphatic sacs engorged, but blood circulation undisturbed. In all the frogs so treated, where unavoidable lacerations of their feet had occurred in manipulating, there oozed from the torn edges minute globules of mercury. The last frog shed his skin in three days after the dose, but otherwise none of them underwent any apparent change in health or vigor. The skin I think must have afforded the main means of exit for the metal. There is not a fragment, however small, of this discarded cuticle which does not exhibit plainly the metallic globules attached to it in great numbers; many hundred microscopic slides may be mounted with the skin from this frog alone, and every slide will reveal fifty or more globules. In the dissecting room of Bennett Eclectic College of this city, a cadaver was exhibited to the students, the skin of which was so covered with mercury that an ordinary pocket magnifier revealed the globules in countless numbers. Dissecting the frog last mentioned I found the stomach coated with the globules, but ten days having elapsed since the dose, no mercury was found between the intestines and the skin except in the dermis, but very probably in the liver. This organ was apparently choked with sacculations of an opaque substance, which at first Mr. E. B. Stuart (who rendered most indispensable assistance) and I took to be pigment granules, but after slicing by the microtome some sections $\frac{1}{20}$ of an inch thick, and the opacity of these spots persisting, careful consideration leads us to think these opaque spots are aggregations of metallic mercury, held in the hepatic channels. In reflected light the unmistakable glint from mercury globules may be caught.

Hoping to discover the courses taken by the metal through the body of the frog, I administered a gram (15.4 gr.) of finely divided mercury, in albumen, to a male frog. In five hours globules appeared on its back. Dissection showed the intestines, renal-portal circulation, heart, kidneys and even the testes, as containing numerous globules of mercury, and the lymphatic passages were beautifully injected with globules much more finely divided. Apparently the lymph channels had chosen the lesser particles, or the metal had undergone further division in absorption into these passages.

CALOMEL.—Adopting Schmidt's analysis of pancreatic juice, as quoted by Dalton, p. 173, (from *Annalen der Chemie und Pharmacie*, 1854, XCII, p. 33,) I found that the materials in the quantities thus given required 21 grams (323 grs.) of the officinal hydrochloric acid to neutralize 143 grams (2200 grs.) of this artificial pancreatic juice. The proportion being as 1 to 7. One part of hydrochloric acid will neutralize one and one-half parts of potassium hydrate. Then the alkalinity of pancreatic juice is to potassium hydrate as 7 to 1.5, or it requires 4.6 times as much pancreatic juice as caustic potash to neutralize the same weight of muriatic acid. Schmidt's quantities being parts of 1000, I am thus enabled to place the alkiliometry of pancreatic juice at 4.6 parts per 1000, which agrees remarkably with Matteneci's estimate of the lymph and chyle alkalinity being equivalent to 4.3 parts per 1000, in terms of potassium hydrate. (Dalton, p. 193.) Carpenter, p. 124, cites Bidder and Schmidt as having estimated the amount of pancreatic fluid daily secreted by man as 7 ounces, (224 grams.) This is equivalent to 10 grams (154 gr) of potassium hydrate and sufficient to reduce 42 grams (647 gr.) of calomel into black oxide of mercury. At least it is safe to presume that an ordinary dose of calomel is converted into black oxide

of mercury as soon as it encounters the pancreatic fluid.

Black oxide of mercury is one of the most unstable compounds; at bodily heat it will yield oxygen and readily be converted into metallic mercury in the presence of deoxidizing substances. Liver sugar, or the glucose formed by pancreatic juice acting upon starchy matter, are quite sufficient to convert the black oxide into metallic mercury, by deprivation of oxygen at bodily temperature.

At this stage we could expect to find calomel acting the same as blue mass, and in general terms this is true, though the liberation of the small amount of chlorine and formation of chlorides of sodium and potassium would of itself accelerate glandular action in the gastro-enteric vicinity. The globules released from calomel average smaller than those in pill mass, though many of the spheres are quite as large.

Parrish's Pharmacy says (p. 290) that "long trituration of calomel increases its power to salivate." This pulverization may cause the liberated globules to be more widely distributed in the alimentary canal and hence prevent any tendency of the lesser globules to form larger ones. In the finer divided state the metal would be able to act more rapidly through the circulation.

At 10 A.M., to a chicken weighing four and a-half pounds, eighteen months old, I gave five grains of calomel. At noon it was sick and very thirsty; 9 P.M. I blew ten grains more calomel into its pharynx, and at 10 o'clock P.M. killed it.

It ejected four ounces of water from its mouth, mixed with the last dose of calomel I had given it, and I recognized black oxide crystals in this liquid which apparently formed above the crop. I did not expect conversion to occur at this point, but it indicates the general tendency of mercurials toward decomposition everywhere in the body instead of a formation of higher salts.

The faeces contained mercury globules. Mercury was distinguishable by the microscope in three out of five parts of the chicken's blood; traces of calomel and black oxide were discernible in the proventriculus and gizzard; a few crystals of the black oxide with a great many globules of the metal were found in the upper intestine, with only metal lower down; the liver contained the metal, while the mesenteries held unmistakably large quantities of the globules, ranging downward in sizes from those usually found in blue mass. The liver globules were small, while those in the mesenteries were large.

Rationally, then, often repeated, small doses of calomel would impress the general system better by allowing reduction and absorption to occur at intervals, insuring complete reduction and absorption, and wide-spread dissemination through circulatory channels. This is no less true of the mercurials in general.

CORROSIVE SUBLIMATE.—"Mercuric salts are converted into mercurous by sugar," p. 98, Vol. II, Miller's Chemistry. According to this view therapeutical doses of the bichloride would change into calomel in the duodenum, but this calomel must by extremely minute division liberate much finer globules of mercury in its further reduction to black oxide and metal. But I am inclined to think that pancreatic conversion of the bichloride into yellow oxide takes place in the duodenum, and this oxide is absorbed into the circulation, where its conversion may occur slowly into the most minute metallic globules. The fact that toxic doses affect mostly the oesophagus and stomach shows that the extra amount of chlorine operates corrosively until the compound is changed by the alkaline pancreatic juice. The transformation of the yellow oxide would occur in the liver, or, if it remained long enough, in the intestines, by the glucose it would encounter, for the yellow oxide is reduced by glucose as well as is the black oxide, only less rapidly.

The bichloride of mercury is not the only substance that will coagulate albumen, nor does it enter into chemical combination with albumen. Excess of the latter will dissolve the bichloride, showing that the whites of eggs alone cannot be relied upon as an antidote for the bichloride of mercury.

I think a better antidotal method would be to at once give an alkali which would convert most of the bichloride into yellow oxide; then give white of egg, with demulcents, to allay the irritation caused by the corrosive chloride. That this corrosive action is due to the chlorine liberated is evident from no other mercuric salt formed with another radical producing the distress peculiar to large doses of the bichloride. Local applications of this salt are apt to be accompanied by severe effects, because the energetic material does not meet with as strong an alkali as it would in the intestines, and hence is not at once converted into a less active form. The blood, however, is alkaline, and would gradually reduce it, but not before wide-spread, strong effects had been experienced. The antiseptic properties of the bichloride are due wholly to its chlorine, and good results are obtained from using it in dilute lotion to heal ulcers. Doubtless this antiseptic property accompanies the mercury, in this soluble form, into the blood, adding to its efficiency as a remedy in syphilis, particularly where the disease is widely disseminated through the body. The sizes of the globules liberated from the yellow oxide formed from bichloride of mercury are incomparably smaller than those from calomel.

To illustrate its exosmotic power, Carpenter, p. 140, mentions that "the bladder of a racoon was filled with the bichloride of mercury and immersed in a solution of potassium iodide; immediately the outside of the bladder was covered with red mercurie biniodide, and inside yellow protiodide." I expect to prove, when my experiments are concluded, that corrosive

sublimate is reduced partly into metal and yellow oxide in the pancreatic fluid, and part of the yellow oxide is reduced by the glucose of the intestine, the remainder undergoing slow conversion in the liver and blood, until the circulation contains the metallic form only, in a state of excessively minute division.

Chloral and chloroform each contain three atoms of chlorine, and resemble mercurie chloride in condensing albumen, and in having irritating and vesicating properties. Bernard believes that chloroform acts by temporarily coagulating the nerve cells. Albumen is given to antidote chlorinated water. Chloride of lime and chlorine are both irritants; the former causes the same kind of gastro-intestinal inflammation as bichloride of mercury. The metallic deposit is found on articles of gold worn next the person after taking mercury in the form of bichloride, as well as when taken in any other form. One-tenth of a grain of red oxide taken twice a day has been used in syphilis, and resembles the bichloride in not causing salivation readily.

CYANIDE OF MERCURY.—Some syphilologists prefer the cyanide to the bichloride, claiming similar results from its use in the same doses, which would argue that it was the mercury and not the material combined with it which exerted medicinal effects. As might be expected from the liberation of cyanogen in the stomach, none of the epigastric pains said to be caused by the bichloride accompany the use of the cyanide. Cyanide is converted into bichloride with hydrochloric acid. This may occur in the stomach, through the free acid there. One of the characteristics of cyanides is that the weakest acids decompose them with liberation of hydrocyanic acid,—its further reduction would be into yellow oxide, and the metal, as described above, under corrosive sublimate. Knapp's test for diabetic sugar with cyanide of mercury shows that sugar is very active in reducing the

metal from this form, and this I believe explains its mode of operating.

GREEN IODIDE OF MERCURY.—Mercurous iodide decomposes by heat in the stomach into mercury globules and mercuric iodide, which is dissolved in the acid fluid of the stomach and further decomposed in the duodenum, precisely as is the bichloride, except with the liberation of iodine instead of chlorine; the yellow oxide from the mercuric salt is further reduced, as is the yellow oxide from the bichloride, into metal. Should the green iodide pass the pylorus unchanged, it would more closely resemble calomel in its effects by resolution into black oxide and mercury, and finally wholly into mercury. The following from the Philadelphia Medical and Surgical Reporter, Vol. XIII, No. 6, p. 127, explains an interesting point in this connection: "It has been frequently observed that the external application of calomel may give rise to severe inflammation of the conjunctiva, if used simultaneously with the administration of iodide of potassium internally. This Dr. Schlafke explains by the formation of iodate and iodide of mercury, which in the presence of common salt or iodide of potassium are soluble and act as caustics. He finds that if iodide of potassium be taken twice daily, in half grain doses, its presence can be constantly detected in the conjunctival sac."

RED IODIDE OF MERCURY.—The biniodide loses its iodine in the pancreatic fluid, though a small amount of the combination may pass into the circulation, there to be decomposed by the alkaline blood. It resembles the bichloride in responding to re-agents, and is as poisonous,—another indication that the mercuric combination owes its activity as much to the *amounts* of the radical liberated in decomposition as to anything else. Topically the effects of concentrated iodine are obtained with mercurialization precisely as a similar application of the bichloride exhibits the localized influence of liberated chlorine.

AMMONIATED MERCURY.—*Hydrargyrum Ammoniatum* is prepared from the bichloride, and to all intents remains corrosive sublimate, combined with ammonia. Its insolubility renders it ineligible for internal use. Pancreatic fluid acts upon it as upon bichloride.

MERCURY WITH CHALK.—*Hydrargyrum cum creta* may be considered as milder than blue mass. It does not contain the same percentage of metal, and the chalk does not maintain separation of the globules, which often are visible to the unaided eye. All the metal in the chalk mixtures I examined was in larger spheres than in blue mass, and the latter is much the better medicine.

THE OXIDES OF MERCURY.—The red oxide, as directed to be prepared by the *Pharmacopœia*, contains nitrate of mercury, and the *Dispensatory* acknowledges that complete purification of the oxide thus made cannot be accomplished without endangering the compound. In consequence it differs from the yellow oxide, though claimed to be an allotropic deutoxide, by its harshness and crystallization, the yellow being amorphous and much milder; but as it contains twice as much oxygen as the black oxide, just as there is twice as much chlorine in the bichloride, the yellow oxide would, in obedience to this general rule, be expected to act more vigorously than the black oxide. The latter has been given in pill form in place of blue mass or calomel, according to Wood in *Dispensatory* (page 1257), and found to have identical effects. Dr. Christisen (page 1531, *ibid*) advises the use of the black oxide in ointment in place of the officinal mercurial ointment.

TURPETH MINERAL.—There has been much discussion over the chemical properties and physiological effects of this preparation. After examining the contradictory statements of all accessible authors, I feel justified in calling it a mixture of mercuric oxide

and sulphate of mercury, $HgO + HgSO_4$. It is an emetic as are other metallic sulphates, and responds to all the tests for the sulphate and oxide of mercury.

ETHIOPS MINERAL.—According to the method of its preparation this substance is a mixture of sulphur and mercury uncombined, cinnabar and metallic mercury with sulphur, and sometimes a sulphate of mercury.

CINNABAR.—Mercuric or red sulphide differs from the other mercuric preparations in being insoluble and undecomposed by alkaline solutions, consequently most of the dose will pass unchanged from the system, though some mercury must be liberated, for it acts rapidly as a mercurial. When used by fumigation, it liberates sulphurous acid gas and mercurial vapor. "In its native state there is reason to believe it has no action at all," p. 721 National Dispensatory. It may thus be regarded as inert, owing to its insolubility. Anything apparently inconsistent with this view may be accounted for by presuming that other forms of mercury accompany the dose as impurities.

OLEATE OF MERCURY.—With a vague idea that all mercurials depended for their efficacy upon their conversion into an oxide in the body, though no valid reason for, or demonstration of, the theory can be found, in 1872 Dr. Marshall suggested the incorporation of mercuric oxide with oleic acid as an eligible substitute for the common ointment. Any chemist, by inspection of Marshall's process, or even later improvements in modes of manufacture of this preparation, can see that the oxide must be destroyed. In fact a precipitation of visible metal occurs, the weight of which is subtracted, plus its oxygen weight, from the original weight of the mercuric oxide used, and the invisible remainder is assumed to be mercuric oxide in oleic acid. Squibb's label on the bottles containing the oleate reads: "This bottle contains 6 per cent" (or some other percentage, as the case may

be) "of mercuric oxide in oleic acid." By decanting off the liquid, further precipitation of the metal, as metal, can be found, and under the microscope beautifully uniform and minute globules of metallic mercury in countless numbers may be seen suspended in the oleic acid. A mechanical mixture of oleic acid and minutely divided mercury I found presented very nearly the same appearance, the globules wanting in uniformity, which I think can be remedied by permitting the mixture to stand some days, allowing the larger globules to precipitate. This settling may prove to be the cause of the minuteness and uniformity of size in Squibb's oleate. So, instead of a mercuric oxide being introduced into the system by inunctions with this preparation, a simple mercurial, reduced to such beforehand, is thus administered and as such it acts. A physician of this city had several applications of the oleate to his axillæ, and soon after, while being dry-cupped, called the attention of Dr. J. S. Jewell (who was treating him for ataxia) to the presence of mercury globules visible in the cupping glass.

The bibromide resembles corrosive sublimate in most respects, and the bromide calomel. Donovan's solution contains the deutoxide and this mention about completes reference to all the compounds used medicinally. All seem to be reduced directly or indirectly to the metallic state. I am not prepared to say positively that the differences in the therapeutical effects of mercury preparations are ascribable mainly to the differences in sizes of the globules, but it looks very much as though this really was the case. This being admitted, we can expect to obtain an intermediate effect between the mercurous and mercuric doses, should we ever use the extremely divided black precipitated mercury from stannous chloride and corrosive sublimate.

Dr. P. W. Van Peyma, in the February number of

the Buffalo Medical and Surgical Journal (p. 290), reviews the points brought forward by Keyes, of New York, in regard to the "tonic treatment" of syphilis. Keyes advocates the use of mercury in small doses long continued. The reviewer claims excellent results from using Keyes' plan of medication, and refers to Dr. J. Shelton Hill's article, in the Maryland Medical Journal for July, as confirmatory of Keyes' observations. Long before becoming acquainted with Keyes' method I had arrived at the conclusion that small doses, about one-sixth of a grain, six times daily, continued for a few months in primary, and lesser doses of finely triturated calomel in subsequent, stages of syphilis, would be conducive of excellent results. My idea being that the trituration would ensure the precipitation of finer divided mercury, and the repeated small doses would thoroughly distribute the drug in its best form for exerting widespread deobstruent effects.

In its action as a parasiticide there can be no doubt that the small globules in some cases, when sucked by parasites into their tubules, cause fatal occlusion; and in other cases, by external contact, effectually asphyxiate insects by choking up their stigmata and tracheæ. Mercury absorbed by plants doubtless kills them by filling up the cellular spaces necessary for the passage of nutrient liquids. Hales found that "during the bleeding season a vine can push up its sap in a glass tube to a height of 21 feet above the stump of an amputated branch." Obviously an interference with this process would be fatal to the life of the plant, and no one can doubt that such a force is capable of pushing the suspended globules well up into the branches. The anthelmintic effects of mercury may be the same as its effects upon other invertebrates and some of the lesser vertebrates.

